REMARKS

Reconsideration of the application is requested in view of the following remarks.

Claims 39-53 remain in this application.

Claims 39-53 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of U.S. Patent No. 6,096,339. Applicants submit herewith a terminal disclaimer over U.S. Patent No. 6,096,339.

Claims 39-53 are rejected under 35 U.S.C. § 103(a) as being unpatentable over *Jao et al.* (U.S. Pat. No. 5,151,338). The Examiner asserts that *Jao* teaches a similar dosage form which demonstrates "a sufficiently uniform drug release that one of ordinary skill in the art can discover a dosage form that does not deviate more than 5% from a mean release rate over a sustained period of time through routine experimentation." Applicants respectfully traverse this rejection as discussed below.

Rejections Under 35 U.S.C.§ 103(a)

Claims 39-53 are rejected under 35 U.S.C. §103(a), as being unpatentable over *Jao, et al.* (US. Pat. No. 5,151,338). In particular, the Examiner asserts that *Jao* discloses the instant invention and that the improvements of the instant invention are obvious and not critical. In particular, the feature of a percentage deviation of not more than 5% from a mean rate of release by the use of controlled particle sizes for the drug and/or hydrophilic polymer, is not critical, thus making the invention obvious.

Applicants respectfully traverse this rejection because Applicant's invention is not *prima facie* obvious from the disclosure of the cited ref rence. In order to be *prima*

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facie obvious over a reference or a combination of references, the reference must describe or teach each of the claim limitations and the references must themselves suggest their particular combination and a reason for that combination without reference to Applicant's application. The references, either taken alone or in combination, are not considered to establish the *prima facie* obviousness of those claims, and the Examiner has not met the burden in properly rejecting the claims.

The Examiner's rejection is respectfully traversed because *Jao* does not motivate towards Applicants' claim element for a uniform rate of release of less than 5% deviation; much less motivate toward Applicants' claim element for use of controlled particle sizes to obtain a more uniform rate of release. The Examiner cites no art that teaches control of particle size to increase uniformity of the rate of release. Applicants' Figures 1-3 demonstrate that control of the particle size of the drug and polymer are critical to reducing the deviation of release rate. Figure 1 illustrates the broad deviation from mean release rate when using drug particle sizes in the broad range of 2 to 900 microns with a polymer where there is more than 25% with particle sizes greater than 250 microns. In contrast, Figure 3 illustrates the pronounced decrease in the variation of the drug release rate when the dosage form comprises a drug size of less than 150 microns with a polymer having particle size of less than 250 micron. Clearly, *Jao* did not address particle size and therefore one skilled in the art could not have been motivated to attain Applicants' claimed less than 5% deviation through control of drug and polymer particle size.

Moreover, if the Examiner is of the belief particle size is not critical to control of the deviation from the mean release rate because it is not taught in *Jao*; there can be

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no "routine experimentation" to control the particle size to reduce the deviation as claimed by Applicants. As the Examiner notes in the First Office Action, "The *Jao et al.* patent does not specifically mention the feature of a percentage deviation of not more than 5% from a mean rate of release, nor does it specifically mention the feature of controlled particle sizes of the drug or the hydrophilic polymer. Therefore, it is the opinion of the examiner that such features are not critical to the function of the claimed invention, and the invention as a whole is *prima facie* obvious." The Examiner's conclusion appears to lack foundation, because limited deviation is a requirement of Applicants' claimed invention. *Jao* appears to concern itself only with the mean release rate overall, and not with the amount of deviation from the mean for individual systems at various rates. It does not follow that because *Jao* did not address deviation, deviation from the mean is not critical.

The Examiner further expresses that "the prior art demonstrates a sufficiently uniform drug release." However, it should be noted that the "sufficiently uniform drug release" in *Jao* is a mean, which does not illustrate the deviation of individual systems at particular rates of release. The present invention provides a release rate for which the deviation in all individual systems and release rates is less than 5%. *Jao* only disclosed the mean release rate, and taught how to obtain that mean release rate, and did not teach how to control the deviation of individual systems at various release rates. While it may be only necessary to look at the mean release rate as in *Jao*, for drug delivery purposes individual systems may require deviation parameters that are within a very narrow range for predictability, or robustness, of the systems. *Jao* does not address the robustness of individual systems and does not teach controlling the

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deviations in mean release rates among individual systems as addressed in the present application.

As the Examiner provides no teaching from *Jao* or any other art to suggest that controlled particle size creates a more uniform rate of release; neither does *Jao* suggest modification of its system to any other rate of release or control of particle sizes. Indeed, the Examiner agrees that *Jao* is silent as to the effect of particle size within the dosage form and is silent on the need for a substantially uniform rate of release that provides less than 5% deviation. Throughout *Jao* only the amount of drug and the amount and molecular weight of the polymer are described. There is no motivation in *Jao* to modify the delivery rate, much less to look to the particle sizes to modify the delivery rate or its uniformity.

Moreover, Applicants define substantially uniform as 100% drug delivery at +/- 5% variation from the norm. Applicants' Application at page 27. The expression "uniform" as defined for the purpose of this invention means a deviation of +/-5% from a constant, 100%, nonvarying delivery. Applicants' Application at page 28. As such, the deviation of +/-5% is a critical component of the invention, which is expressly incorporated into the claims and supported by the application. As such, there is no motivation in *Jao* for substantially uniform delivery as claimed by Applicants.

Therefore, it would not have been *prima facie* obvious to a person of ordinary skill in the art at the time of the invention to prepare a controlled release dosage form utilizing controlled drug and polymer granule sizes to provide for a substantially uniform rate of release having a less than 5% deviation from the constant.

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For these reasons, Applicants assert that the rejection of claims 39-53 is not appropriate and withdrawal of the rejection is respectfully solicited. Applicants respectfully submit that Claims 39-53 are novel and not obvious over the art cited and are in a position for allowance.

Reconsideration of the application is respectfully requested. Please direct any questions to the undersigned attorney at (650) 564-5171.

Respectfully submitted,

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Enclosures:

1. Terminal Disclaimer

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